UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/487,979	01/20/2000	Boris Skurkovich	0011-1U9	3797

28977 7590 01/28/2004

MORGAN, LEWIS & BOCKIUS LLP
1701 MARKET STREET
PHILADELPHIA, PA 19103-2921

EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/487,979	SKURKOVICH ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42,45 and 48-50* is/are pending in the application.

4a) Of the above claim(s) *45 and 48-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1644.

2. Applicant's amendment, filed (9/4/03), has been entered.

Claims 42, 45, 46 and 48-50 are pending in the instant application.
Claims 45 and 48-50 have been withdrawn from consideration.
Claims 42 and 46 are currently under examination.
Claim 46 has been amended.

Claims 1-41 and 43-44 have been canceled previously.

3. Upon reconsideration, the previous rejection under 35 U.S.C. § 112, first paragraph, has been withdrawn and New Grounds of Rejection have been set forth herein.

4. The priority date of the instant application is USSN 08/771,831, filed 12/23/96, now U.S. Patent No. 5,88,511.

5. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. This is a rejection under 35 USC § 112, first paragraph, "written description" (and not new matter).

Claim 46 is rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

There is insufficient written description encompassing ""allelic and species variants thereof" because the relevant identifying characteristics such as structure of other physical and/or chemical characteristics of said "allelic and species variants thereof" are not set forth in the specification as-filed, commensurate in scope with the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Thus, the specification fails to describe these DNA sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicant is relying upon certain biological activities and the disclosure of a limited representative number of species to support an entire genus. The instant invention encompasses employing any antibody that binds any "allelic or species" of "gamma interferon, alpha interferon or tumor necrosis factor alpha", yet the instant specification and the priority applications do not provide sufficient written description as to the structural features of any "allelic or species" of "gamma interferon, alpha interferon or tumor necrosis factor alpha" and the correlation between the chemical structure and the function of the genus of "allelic or species" variants of "gamma interferon, alpha interferon or tumor necrosis factor alpha". The reliance on the disclosed limited examples of the known human "gamma interferon, alpha interferon or tumor necrosis factor alpha" factors/cytokines in the specification as-filed and the priority applications do not support the written description of any "allelic or species" of "gamma interferon, alpha interferon or tumor necrosis factor alpha".

Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). In the absence of sufficient guidance and direction to the structural and functional analysis, applicant's reliance upon the certain known structures of alpha interferon, gamma interferon and tumor necrosis factor alpha disclosed in the specification as-filed and the priority applications does not appear to provide sufficient written description for any "allelic or species" of "gamma interferon, alpha interferon or tumor necrosis factor alpha".

Applicant is relying upon certain properties and the disclosure of a limited representative number of species to support an entire genus of "an antibody that is specific for the "alleleic or species" of "gamma interferon, alpha interferon or tumor necrosis factor alpha".

For example, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document).

For example, Li et al. (PNAS 77: 3211-3214, 1980) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document).

The instant claims do not provide sufficient structural and functional characteristics coupled with a known or disclosed correlation between function and structure. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus of "alleleic or species" of "gamma interferon, alpha interferon or tumor necrosis factor alpha".

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

In the absence of structural characteristics that are shared by members of the genus of "alleleic or species" variants of "gamma interferon, alpha interferon or tumor necrosis factor alpha"; one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genuses or "alleleic or species" variants of "gamma interferon, alpha interferon or tumor necrosis factor alpha". See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

In the absence of structural characteristics that are shared by members of the genus of "alleleic or species" variants of "gamma interferon, alpha interferon or tumor necrosis factor alpha"; one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

7. Claim 46 is objected to in that the proper spelling of "alleleic" is "allelic".
Applicant is required to amend the claim accordingly.

8. Claim 46 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 46 is indefinite in that the antecedent basis of "alleleic or species variants thereof" is unclear and confusing.
Applicant is invited either to amend the claim accordingly or, at least, to clearly indicate which terms are the antecedent basis of "alleleic or species thereof".

B) Claims 46 is indefinite in that the singular form "biologically active fragment" lacks proper antecedent basis to the plural form of "biologically active fragments".

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 42 and 46 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Mak (US Patent No. 6,190,691) AND Skurkovich et al. (Medical Hypotheses 42: 27-35, 1994) in further view of Bucala et al. (WO 94/26307).

Mak teaches that it was known at the time that a number of cytokines, including interferons and tumor necrosis factors contribute to inflammation, which can be regulated by anti-inflammatory drugs (see Background of the Invention on columns 1-2). Mak teaches methods of treating pathological conditions which are mediated by these inflammatory cytokines, and, in particular, teaches methods of treating AIDS or HIV-positive patients with anti-TNF alpha antibodies (see Summary of the Invention on columns 3-4 and Detailed Description of the Invention, including columns 9-10).

Mak et al. differs from the claimed methods by not disclosing the use of anti-interferon antibodies in combination with anti-TNF alpha antibodies to treat patients with AIDS or HIV-infected patients.

Skurkovich et al. teach that the neutralization of hyperproduced interferons and certain other cytokines can dampen the production or biological activity of these factors as a therapeutic approach to the management of these chronic diseases such as AIDS (see entire document, including the Abstract). In addressing the cytokines involved in AIDS and that interferon and TNF are pathogenetic triggers in AIDS, this reference notes that the production of interferon induces the synthesis of TNF and its receptors and stimulates viral replication (see page 29, column 2, paragraph 1 and page 30, column 1, paragraph 1). Skurkovich et al. teach the use of an antibody to IFNα and IFNγ as a method of treatment (page 29, column 1, lines 21-23). Skurkovich et al. set forth Conclusions and Practical Recommendations for treating AIDS, including neutralizing IFNα, IFNγ and TNF (see pages 31-33).

Although Skurkovich et al. teach removing IFNα, IFNγ and TNF in AIDS via absorbents, Skurkovich et al. differs from the claimed methods by not explicitly teaching administering the combination of antibodies to IFNα, IFNγ and TNF to HIV infected patients per se.

Bucala et al. teach methods of treating various conditions involving cytokine-mediated cytotoxicity by administering combinations of therapies that antagonize initiators of cytokine-mediated toxicity, including anti-TNFα and anti-IFNγ antibodies (see entire document, including pages 7-8, overlapping paragraph and Claim 27 on page 115).

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Mak et al. and Skurkovich et al. to target and neutralize IFNα, IFNγ and TNF in AIDS or HIV-infected patients by administering a combination of antibodies to IFNα, IFNγ and TNF. In addition to the teachings of Skurkovich et al. of targeting IFNα, IFNγ and TNF in AIDS or HIV-infected patients, Bucala et al. teach combining anti-interferon and anti-TNF antibodies to antagonize the effects of cytokine-mediated effects. One of ordinary skill in the art at the time the invention was made would have been motivated to combine antibodies to IFNα, IFNγ and TNF in treating AIDS or HIV-infected patients, given the contribution of each of these to the pathologic manifestations in such patients and the teachings to treat such patients with each of these antibodies to IFNα, IFNγ and TNF. Such antibodies to IFNα, IFNγ and TNF would target alleleic or species variants of IFNα, IFNγ and TNF, given that the antibodies to IFNα, IFNγ and TNF would bind the same epitopes common to alleleic or species variants of IFNα, IFNγ and TNF. It was prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306.

Phillip Gambel

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
January 15, 2004